Detailed Visual Cortical Responses Generated by Retinal Sheet Transplants in Rats with Severe Retinal Degeneration.

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Public Summary:
Cell Transplant Restores Vision in Rats: Sheets of fetal cells integrate into the retina and generate nearly normal visual activity in the brains of blind rats, reports new research published in J Neurosci. Degeneration of the retina as a result of age or progressive eye disease damages the light-detecting cells necessary for accurate vision. Current treatments can only help protect existing cells from further damage and are ineffective during late stages of disease once these cells are gone. Retinal sheet transplants have been demonstrated in prior animal and human studies, but their ability to restore complex vision has not yet been assessed. Measuring the response of neurons in the primary visual cortex, David Lyon and colleagues demonstrate rats with severe retinal degeneration that received donor cells became sensitive to various attributes of visual stimuli, including size, orientation, and contrast, as early as three months following surgery. The study represents an important step forward in combating age- and disease-related vision loss in human adults.

Scientific Abstract:
To combat retinal degeneration, healthy fetal retinal sheets have been successfully transplanted into both rodent models and humans, with synaptic connectivity between transplant and degenerated host retina having been confirmed. In rodent studies, transplants have been shown to restore responses to flashes of light in a region of the superior colliculus corresponding to the location of the transplant in the host retina. To determine the quality and detail of visual information provided by the transplant, visual responsivity was studied here at the level of visual cortex where higher visual perception is processed. For our model, we used the transgenic Rho-S334ter line-3 rat (both sexes), which loses photoreceptors at an early age and is effectively blind at postnatal day 30. These rats received fetal retinal sheet transplants in one eye between 24 and 40 d of age. Three to 10 months following surgery, visually responsive neurons were found in regions of primary visual cortex matching the transplanted region of the retina that were as highly selective as normal rat to stimulus orientation, size, contrast, and spatial and temporal frequencies. Conversely, we found that selective response properties were largely absent in nontransplanted line-3 rats. Our data show that fetal retinal sheet transplants can result in remarkably normal visual function in visual cortex of rats with a degenerated host retina and represents a critical step toward developing an effective remedy for the visually impaired human population.SIGNIFICANCE STATEMENT Age-related macular degeneration and retinitis pigmentosa lead to profound vision loss in millions of people worldwide. Many patients lose both retinal pigment epithelium and photoreceptors. Hence, there is a great demand for the development of efficient techniques that allow for long-term vision restoration. In this study, we transplanted dissected fetal retinal sheets, which can differentiate into photoreceptors and integrate with the host retina of rats with severe retinal degeneration. Remarkably, we show that transplants generated visual responses in cortex similar in quality to normal rats. Furthermore, transplants preserved connectivity within visual cortex and the retinal relay from the lateral geniculate nucleus to visual cortex, supporting their potential application in curing vision loss associated with retinal degeneration.